

AD _____

GRANT NUMBER DAMD17-94-J-4343

TITLE: Breast Cancer Tissue Repository

PRINCIPAL INVESTIGATOR: J. Dirk Iglehart, M.D.

CONTRACTING ORGANIZATION: Duke University
Durham, North Carolina 27710

REPORT DATE: September 1996

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

19970220 091

DTIC QUALITY INSPECTED 1

REPORT DOCUMENTATION PAGE

*Form Approved
OMB No. 0704-0188*

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (<i>Leave blank</i>)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED	
	September 1996	Annual (1 Sep 95 - 31 Aug 96)	
4. TITLE AND SUBTITLE		5. FUNDING NUMBERS	
Breast Cancer Tissue Repository		DAMD17-94-J-4343	
6. AUTHOR(S)			
J. Dirk Iglehart, M.D.			
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)		8. PERFORMING ORGANIZATION REPORT NUMBER	
Duke University Durham, North Carolina 27710			
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)		10. SPONSORING/MONITORING AGENCY REPORT NUMBER	
Commander U.S. Army Medical Research and Materiel Command Fort Detrick, Frederick, MD 21702-5012			
11. SUPPLEMENTARY NOTES			
12a. DISTRIBUTION / AVAILABILITY STATEMENT		12b. DISTRIBUTION CODE	
Approved for public release; distribution unlimited			
13. ABSTRACT (<i>Maximum 200</i>)			
<p>During the preceding year, the Duke Breast Cancer Tissue Repository collected breast cancer tissue from 126 patients undergoing surgery for a primary breast cancer. This compares to 124 entries in the first year of the repository. As before, nearly all of these tissues were both snap frozen in liquid nitrogen and embedded in gelatin for special applications. In 120 patients, serum and peripheral white cells were collected prior to surgery. An additional bank of normal plasma and white cells has been collected during the previous year. The Department of Defense Repository has provided tissues and blood to multiple investigators within Duke and in other U.S. institutions. The Repository has supported the Duke Specialized Project of Research Excellence (SPORE) and the Duke Comprehensive Cancer Center in a joint effort to establish a breast cancer genetics program at Duke. For this endeavor, the Repository has provided phlebotomy and blood storage for research studies looking at new genes and genetic loci in candidate families.</p>			
14. SUBJECT TERMS Humans, Breast Cancer, Tissue, Serum, Primary Metastatic, Anatomical Samples, Plasma			15. NUMBER OF PAGES
			8
16. PRICE CODE			
17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the US Army.

N/A Where copyrighted material is quoted, permission has been obtained to use such material.

N/A Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

YAS For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

INIA In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

In the conduct of research involving hazardous organisms,
the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.


Dr. Dehatum
PI - Signature Date 10/2/90

Table of Contents
DAMD17-94-J-4343
Breast Cancer Tissue Repository

Statement of Purpose, Introduction, Body.....	3
Inventory Summary.....	3
Summary of Usage.....	4
Expanding Roles.....	4
Relation to the SPORE and Cancer Center.....	5
Conclusions.....	5

Introduction

The purpose of the Breast Tissue Repository at Duke University is to provide a resource of tissue from breast cancer patients, patients with benign breast diseases, and normal material from women undergoing cosmetic surgery. In addition, control plasma and genomic DNA from normal individuals is provided to researchers at Duke and in other US institutions. The Repository serves investigators within Duke University and collaborators at other institutions, depending upon availability and priority. The Repository is intended for high-volume use and is not used as an archive of clinical material. Exploratory molecular and genetic investigations are the most appropriate use of this facility; detailed follow-up for clinical correlation is not provided. The Repository will collect material in a tailor-made fashion for special applications or studies initiated by Duke investigators.

During the past two years, the Breast Tissue Repository has grown and has become a well used resource for Duke investigators. Selected researchers from other institutions have requested material. We were successful in our application for a Specialized Program of Research Excellence (SPORE) in Breast Cancer which began in October of 1995. This program has catalyzed breast cancer research at Duke and has opened up a variety of new applications for the Repository.

Body of Renewal

Inventory Summary

As of September, 1996 the Repository has collected samples from 1055 patients. This includes samples from 704 patients banked since 1988 and an additional 351 patients since the Repository was funded by the Department of Defense. Several additional features have been added since DOD funding began last year: 1) Two hundred samples have been frozen in gelatin (OCT) for in-situ applications, 2) Normal white blood cells are now available for each tumor banked, 3) A plasma repository has been added which includes both pre-operative and follow-up blood. This plasma bank now has 285 patient entries. The following table displays the range of histologies which have been collected during the past two years of funding.

Table 1. Histology of samples collected between 9-1-94 and 9-1-96

Histology	Number Acquired
Normal	25
Invasive Ductal (NOS)	148
Invasive Lobular	20
Specialized Histologies (medullary, etc)	9
Benign (eg, fibroadenoma)	1
Pure noninvasive (DCIS)	9
Miscellaneous (recurrent, etc)	28

Summary of Usage

Usage of the Repository remains high and has increased since the Duke SPORE was funded. Overall, several thousand samples have been distributed to investigators. In two cases, we have done specialized collections for specific studies. Dr. Kent Weinhold was provided with fresh tumor samples and heparinized blood from 83 patients over the past 2 years in order to isolate tumor infiltrating lymphocytes and peripheral T and B cells. Drs. Andrew Futreal and Joellen Schildkraut have received blood from kindreds ascertained through the SPORE which are neither BRCA1 or BRCA2 linked. These families are part of an effort, supported by supplemental funds from the NCI to the Duke Cancer Center, to isolate BRCA3 and other susceptibility genes for breast cancer. These studies have just begun, but will accelerate during the coming year. Dr. Randy Jirtle has been provided with freshly drawn and heparinized blood to determine plasma levels of TGF β ; thus far, Dr. Jirtle has received 276 pre-operative and post-operative blood samples. Dr. H. Kim Lyerly has received 17 fresh tumors for isolation of tumor cells and infection with vectors expressing cytokine genes. The following table summarizes the routine usage of Repository material.

Table 2. Summary of Routine Usage during the past year (Sept 95-Sept 96)

Investigator	Affiliation	Number of Samples Provided
Dr. Jeff Marks	Surgery, Duke	450
Dr. Andrew Futreal	Surgery, Duke	54
Dr. Robert Ochs	Scripps Institute	150
Dr. Randy Jirtle	Radiation Oncology, Duke	140
Dr. Kent Weinhold	Surgery, Duke	45
Dr. Andrew Berchuck	Ob-GYN, Duke	76
Dr. Alex Miron	Surgery, Duke	60
Dr. Laura Hale	Pathology, Duke	11
Dr. Kim Lyerly	Surgery, Duke	6
Dr. Charles Greenberg	Medicine, Duke	70

Expanding Role for the Department of Army Repository at Duke

As noted above, the Repository has assisted the Cancer Center and the SPORE in Breast Cancer with research in the molecular genetics of breast cancer. Personnel in the Repository assisted in family recruitment (phone interviews), obtained general research consent for blood storage and obtained blood samples. This activity contributed to the discovery of BRCA2 by investigators at Duke and collaborating institutions in November of 1995. As part of the SPORE, we are offering genetic testing to large numbers of women who have a high "prior probability" of carrying a mutation in BRCA1 or BRCA2. The phlebotomist from the Repository is drawing the blood for this research. We expect that several families will be identified in which there is neither a mutation in BRCA1 or BRCA2. In these kindreds, linkage might turn up new susceptibility genes. To conduct

linkage and gene discovery in these families, the Repository will assist our genetic researchers in obtaining complete family histories, finding family members and obtaining blood after informed consent. In each case, expert genetic counseling will be provided by the Cancer Center and SPORE personnel so that Repository personnel will only need to provide consent for the actual phlebotomy. However, the Repository will assist with family ascertainment, bleeding drawing, transportation of blood samples, storage and preparation.

At this point, testing for BRCA1 and BRCA2 has begun. We will be testing families with high prior probabilities first and will likely begin to identify candidate kindreds for new gene discovery by the end of this year. I expect this activity will increase during the rest of next year.

Relation of the Army Repository to the Duke SPORE in Breast Cancer and to the Comprehensive Cancer Center Genetic Supplement

The NIH requires that each SPORE in Breast Cancer include a Tissue Repository which must be a line-item in each SPORE budget. We proposed to delete this line item and rely upon the Army Repository entirely; this was administratively refused. Therefore, we proposed an addition to the Army Repository to provide specialized services peculiar to the SPORE. These peculiar services provided by the SPORE tissue bank are as follows: 1) provision of established cell lines to investigators, 2) attempt to culture breast cancer in-vitro and in immune compromised animals, 3) provision of animals bearing human tumor grafts from established cell-lines, and 4) provision of a specialized window-chamber preparation to investigators studying aspects of breast tumor physiology (eg., angiogenesis, macromolecule delivery, etc.). We recently expanded the tissue service within the SPORE to include an animal facility for pre-clinical drug testing by re-budgeting from other sources. In no way does the tissue bank within the SPORE overlap with the Army-sponsored Repository. However, the Army Repository supports and augments the SPORE-sponsored bank and SPORE research.

The Cancer Center recently received notice of supplemental funding to begin a genetics program at Duke, concentrating on breast cancer genetics. This funding will support genetic epidemiology, family ascertainment, a familial data-base, and laboratory-based linkage and cloning projects. The Army Repository is in an ideal position to support this new research effort by providing phlebotomy services, assisting in family member identification and in the storage and handling of blood samples. The Army Repository complements this research perfectly.

Conclusions

The Department of the Army Breast Cancer Tissue Repository at Duke University is a high-volume resource which has served investigators in a variety of departments and Programs within Duke Medical Center. In future years, the Repository will serve the new genetic research within the Duke SPORE in Breast Cancer and within the Cancer Center. The Repository has provided specialized collection services to investigators who require

freshly collected and sterile samples, blood from normal control women and blood for gene discovery research. The Repository interdigitates with the SPORE Core Tissue Resource by providing clinical tissues for storage and distribution (Army Repository) while the SPORE provides cell and animal resources for local investigators.

Submitted by

A handwritten signature in black ink, appearing to read "J. Dirk Iglehart". The signature is fluid and cursive, with a large, stylized 'J' at the beginning.

J. Dirk Iglehart, M.D.
Principal Investigator